UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/067,638 | 04/28/1998 | LEX M. COWSERT | ISIS-2960 | 1414 |

32650 7590 08/25/2003

WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE - 46TH FLOOR
PHILADELPHIA, PA 19103

| EXAMINER |
|---|
| MARSCHEL, ARDIN H |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1631 | 39 |

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/067,638 | COWSERT ET AL. | |
| | Examiner | Art Unit | |
| | Ardin Marschel | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *83-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *83-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *35* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission, filed on 5/16/03, has been entered.

It is acknowledged that the Petition to withdraw the instant application from allowance has been granted.

Applicants' submission, filed 5/16/03, has been fully considered and they have resulted in the below set forth set of rejections. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

## VAGUENESS AND INDEFINITENESS

Claim 84 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 84 is vague and indefinite due to containing abbreviations without the full name therewith. Such abbreviations are unclear without a full name, for example, in

parentheses with each such abbreviation. Clarification is requested via clearer claim wording.

**PRIOR ART**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 83 and 85-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. (P/N 5,463,564); taken in view of Hyndman et al. [Biotechniques 20(6):1090(1996)] and Nickerson et al. [PNAS 87 :8923(1990)].

The instant claims are directed to a system made up of a computer network for virtual oligonucleotide design, automated synthesis via an automated synthesizer of oligonucleotides, and an apparatus which identifies members of the oligonucleotides as synthesized via computer-controlled PCR or ELISA.

Agrafiotis et al. describes an overall system with the above instantly claimed and described components therein in Figure 2. Desired activity/properties for chemical reagents are utilized in a synthesis control generator where virtual design takes place and then robotically synthesized followed by an apparatus for the analysis of said chemicals regarding structure-activity. Reagents that are suggested to be designed etc. are suggested in column 1, lines 16-30, to include bioactive compounds etc. Biological testing of a subset of identified compounds out of a huge library is described in column 1, lines 39-45. The invention of Agrafiotis et al. is summarized in columns 3-4 as being directed to an process of forming a diverse database of compounds which may be selected from, synthesized, and analyzed for desired activity. The prediction of activity for the design of candidate compounds from molecular features therein is generically motivated and suggested in the reference in column 17, line 6, through column 19, line 9, wherein the last paragraph describes the selection of a final set of compounds which are highest ranking in desired characteristics as a result of the computational selection processes as described in said columns 17-19, thus motivating, summarizing, and suggesting virtual compound design and selection.

Hyndman et al. Summarizes the desirability of oligonucleotides as essential components for a variety of biological procedures on page 1090 in the INTRODUCTION section, inclusive of nucleic acid detection or antisense inhibition of gene expression (as in the last 2 lines of instant claim 86). Thus motivated Hyndman et al. describes the designing of oligonucleotides in a computer system via corresponding software as is summarized also in the abstract. Additional motivation to utilize such virtual

oligonucleotide design is the disclosure therein of its computer system's ability to optimize such a procedure as set forth in the title. The HYB simulator of Hyndman et al. is described on page 1091, in the first paragraph of the section entitled " PRINCIPLE OF HYBsimulator" as selecting probes from a database which describes the reducing of members of a virtual library as also described in instant claim 83, lines 3-7, for example. The remainder of Hyndman et al. details various aspects of the probe oligonucleotide procedures directed to optimizing hybridization of such probes with target nucleic acid, such as DNA etc. for the detection of such targets within samples of nucleic acid such a commonly extracted as a mixture for analysis. Hyndman et al. Specifically suggests and motivates PCR usage of designed oligonucleotides on pages 1094 and 1096, in the section entitled "Basic PCR".

Nickerson et al. Describes the automated analysis of DNA for diagnostics via PCR as well as an ELISA assay in the title and abstract. The introductory discussion on page 8923 of Nickerson et al. summarizes hybridization based usage of oligonucleotides for DNA diagnosis wherein the oligonucleotides hybridize to a target DNA either with perfect complementarity or with mismatches. The desired primers and probes are further described as being designed for variants etc. of DNA targets on page 8924 in the section entitled "Amplification Primers and Ligation Probes" wherein functional gene targets within a sample are summarized. A robotic and thus automatic workstation apparatus is described on page 8924 with assays also performed in such a workstation in the first column. Automated synthesis of the oligonucleotides utilized therein is described on page 8923, second column, in the section entitled

"Oligonucleotides" wherein a well known automatic synthesizer is utilized and referred to as an "Applied Biosystem 380A DNA synthesizer" as also instantly claimed. It is noted also that a plate reader which determines optical density as also an option in the last 3 lines of instant claim 85 is described as a second apparatus on page 8924, last 2 sentences of the section entitled "Ligation Assays".

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to be guided by the generic design, synthesis, and testing description of Agrafiotis et al. to assemble such a system from components which perform these tasks for a desired compound type. Hyndman et al. Summarizes the plurality of reasons for oligonucleotide usage and suggests therein an optimized virtual design system which selects desired oligonucleotides from a larger database for primer, probe, etc. usage including specifically PCR procedures. Such a design system as in Hyndman et al. is thus motivated and suggested to provide oligonucleotide primers and probes that will optimally hybridize to desired targets as described and suggested in Nickerson et al. wherein testing via automatic apparatus inclusive of PCR and ELISA tests are thereafter described. Nickerson et al. Also describes the automatic synthesis of the primers and probes utilized therein as is also claimed. Thus, the overall system of Agrafiotis et al. with specific motivation and descriptions of usable components for oligonucleotide compound design, synthesis, and testing as in Hyndman et al. and Nickerson et al. results in the practice of the instantly claimed invention.

Claims 83-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrafiotis et al. (P/N 5,463,564); taken in view of Hyndman et al. [Biotechniques

20(6):1090(1996)] and Nickerson et al. [PNAS 87 :8923(1990)]; taken further in view of either of Albertsen et al. (P/N 5,352,775) or Cutting et al. (P/N 5,407,796) regarding certain specific functional target regions in instant claim 84.

The combination of Agrafiotis et al.; Hyndman et al.; and Nickerson et al. has been described above. This combination motivates and suggests targeting functional genetic or nucleic acid regions but lacks description of such specific regions as listed in instant claim 84.

Cutting et al. in column 3, lines 8-18, describes a target mutation site at a stop codon with motivation to prepare probes for such a site generically set forth in the abstract.

Albertsen et al. In column 25, lines 31-63, describes a start or initiator codon delection mutation for which primers are designed for detection in a PCR analysis.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to target specific functional sites as described by either of Cutting et al. or Albertsen et al. for hybridization/PCR analysis which are desired targets that may be utilized as functional targets in the generally motivated and suggested systems of Agrafiotis et al.; Hyndman et al., and Nickerson et al. thus resulting in the instant claim embodiments as specifically cited in claim 84 but also deemed species within the other pending claims.

## PROVISIONAL OBVIOUSNESS-TYPE DOUBLE PATENTING

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 83 and 85-87 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 55, 56, 58-72, 74-87, and 99-102 of copending Application No. 09/295,463. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to common embodiments for the virtual design of compounds targeted to functional nucleic acid targets with synthesis and robotic or automatic assay thereof, however, with respective claims of differing scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is

(703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 22, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER

| Notice of References Cited | Application/Control No. 09/067,638 | Applicant(s)/Patent Under Reexamination COWSERT ET AL. | |
|---|---|---|---|
| | Examiner Ardin Marschel | Art Unit 1631 | Page 1 of 1 |

**U.S. PATENT DOCUMENTS**

| * | | Document Number Country Code-Number-Kind Code | Date MM-YYYY | Name | Classification |
|---|---|---|---|---|---|
| | A | US-,407,796 | 04-1995 | Cutting et al. | 435/6 |
| | B | US-5,352,775 | 10-1994 | Albertsen et al. | 536/23.1 |
| | C | US- | | | |
| | D | US- | | | |
| | E | US- | | | |
| | F | US- | | | |
| | G | US- | | | |
| | H | US- | | | |
| | I | US- | | | |
| | J | US- | | | |
| | K | US- | | | |
| | L | US- | | | |
| | M | US- | | | |

**FOREIGN PATENT DOCUMENTS**

| * | | Document Number Country Code-Number-Kind Code | Date MM-YYYY | Country | Name | Classification |
|---|---|---|---|---|---|---|
| | N | | | | | |
| | O | | | | | |
| | P | | | | | |
| | Q | | | | | |
| | R | | | | | |
| | S | | | | | |
| | T | | | | | |

**NON-PATENT DOCUMENTS**

| * | | Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages) |
|---|---|---|
| | U | |
| | V | |
| | W | |
| | X | |

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.